REMARKS

This Amendment and Response is submitted in response to the Office Action mailed July 29, 2004 (Office Action). A supplemental Information Disclosure statement (IDS) accompanies this response. A check for $1200 for the fee for a three-month extension of time ($1020) and for the fee for filling the supplemental IDS ($180) accompanies this response. Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 06-1050. If a Petition for Extension of Time is needed, this paper is to be considered such Petition.

Claims 1-77 and 80-107 are pending. Claims 78 and 79 are cancelled herein without prejudice or disclaimer. Claims 1-3, 5-7, 9, 11-18, 20-21, 23, 25, 27, 29-30, 32, 35, 49-50, 58, 60-74, 80-88, and 90-107 are amended herein clarity. Support for amendments is found throughout the specification and, in particular, in the respective claims as originally filed. Claim 1 is amended to include the recitation –a modulator for a member of the androgen receptor family–, basis for which is found throughout the specification (for example, see page 45, lines 19-20). Claims 1, 32, and 50 have also been amended to remove certain substituents from R^{18}. Support these amended claims is found throughout the specification, for example at page 16, lines 7-10 and page 26 and in the claims as originally filed. Therefore, no new matter has been added by reason of these amendments.

Informalities

A. Incorporation By Reference

The Examiner objects to incorporation by reference of certain material in the specification. Office Action at page 2. Specifically, the Examiner alleges that references at page 110, line 22 and at page 111, lines 25-26 describing the "co-transfection assay" constitute essential material. This rejection is respectfully traversed.

Incorporation by reference of "essential material" and "nonessential material" is discussed in the MPEP at MPEP § 608.01(p)(I). For example, MPEP § 608.01(p)(I)(A) states:

> "Essential material" is defined as that which is "necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112)" ...
>
> Nonessential subject matter is subject matter referred to for purposes of indicating the background of the invention or illustrating the state of the art.

MPEP § 608.01(p)(I) also states that

> Nonessential subject matter may be incorporated by reference to (1) patents or applications published by the United States or foreign countries or regional patent offices, (2) prior filed, commonly owned U.S. applications, or (3) non-patent publictions....

The references objected to by the Examiner are Evans *et al.* on page 110, line 22, US Pat. Nos. 4,981,784 and 5,071,773 to Evans *et al.* on page 110, lines 25-26 and Berger *et al.* on page 111, lines 8-9. These references describe a co-transfection assay that mimics an *in vivo* system in the laboratory. One of skill in the art will recognize that the assay described in the references can be used to in assessing certain compounds, but is not subject matter claimed in the application.

The references illustrate the state of the art at the time of filing the original application with respect to assays available for assessing *in vivo* pharmacology of various compounds, including the claimed subject matter. For example, Evans *et al.* (U.S. Pat. No. 5,071,773) teaches that its bioassays are useful for evaluating whether compounds are functional ligands for receptor proteins (see claim 2 and Abstract). The ability of a compound or composition to modulate the transcriptional ability of intracellular receptors including RXRs may be measured by any of the assays known to those of skill in the art, including but not limited to the co-transfection (cis-trans) assays. Such assays are described in, e.g., U.S. Pat. Nos. 4,981,784, 5,071,773, 5,298,429, 5,506,102, as well as in WO89/05355, WO91/06677, WO92/05447, WO93/11235, WO93/23431, WO94/23068, WO95/18380 and CA 2,034,220. Heyman *et al.* (Cell, 68:397-406 (1992)) also teaches such assays. Thus, because the references cited by the Examiner as allegedly being incorrectly incorporated by reference illustrate the state of the art, the references are nonessential material, and are properly incorporated by reference under MPEP § 608.01(p)(I).

Even without the incorporated references, the application describes the assay with sufficient detail to allow one of skill in the art to practice the assay. The Examiner's attention is directed to the *Biological Examples* section of the application on page 110, line 20 through page 114, line 5. For example, Example B of the *Biological Examples* section, page 112, line through page 114, line, entitled *Co-transfection assay*, provides a detailed description of the assay. The references clearly illustrate that one of skill in the art could use such assays to assess the claimed compounds.

The Examiner cites to *In re Hawkins* to support the objection that the above-noted references are improperly incorporated by reference in the application. This is inapt. In *In re Hawkins*, the incorporated material is deemed essential subject matter. The incorporated material described how to make starting materials, which the Board found were necessary to make the claimed compounds. See *In re Hawkins*, 179 U.S.P.Q. 157, 165. As discussed above, the references illustrate the state of the art at the time of filing the application. Hence,

the references are nonessential material and are properly incorporated by reference. Applicant respectfully requests that the objection be withdrawn.

B. Typographical Errors

The Examiner notes that a typographical error appears on page 83 of the specification. Applicant has corrected the error by the amendment of the specification herein.

The Examiner notes that claim 102 was incorrectly numbered "101" and indicates that the second claim numbered "101" has been renumbered as "102" under 37 C.F.R. § 1.126. Applicant has corrected the error and will use the correct designation in all subsequent submissions.

THE REJECTION OF CLAIMS 1-55 AND 58-107 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-55 and 58-107 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly being broader than the enabling disclosure because it alledgely would require undue experimentation to make and use all of the compounds within the scope of the claims. The Examiner relies on the factors set forth in *In re Wands* to reach this conclusion. This rejection is respectfully traversed.

RELEVANT LAW

The test of enablement is whether one skilled in the art can make and use what is claimed based upon the disclosure in the application and information known to those of skill in the art without undue experimentation. *United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). A certain amount of experimentation is permissible as long as it is not undue. A patent application need not teach, and preferably omits, what is well known in the art. *Spectra-Physics, Inc. v. Coherent , Inc.*, 3 USPQ2d 1737 (Fed. Cir. 1987). Indeed, "not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted." *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332. Showing every combination of substituents is unnecessary.

A considerable amount of experimentation is permissible, particularly if it is routine experimentation. The amount of experimentation that is permissible depends upon a number of factors, which include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. *See, Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int'f 1986); see also *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

ANALYSIS

Applying the above-noted factors to the instant facts reveals that the amount of experimentation is not undue.

1. The scope of the claims.

Claim 1 is directed to a compound having the formula of I, II, III or IV, and claims 2-57 ultimately depend from claim 1 and are directed to various embodiments thereof. Claim 58 is directed to a pharmaceutical composition including a pharmaceutically acceptable carrier and a compound of formula I, II, III or IV, and claims 59-77 ultimately depend from claim 58 and are directed to various embodiments thereof. Claim 80 is directed to a method of treating an individual having a condition mediated by an androgen receptor that includes administering to the individual a pharmaceutically effective amount of a compound of any one of claims 1, 56, or 57. Claims 81-86 depend from claim 80 and are directed to various embodiments thereof. Claim 87 is directed to a method of modulating an androgen receptor in an individual that includes administering to the individual an androgen receptor modulating effective amount of a compound of any one of claims 1, 56, or 57. Claims 88-106 ultimately depend from claim 87 and are directed to various embodiments thereof. Claim 107 is directed to a method of treating cancer that includes administering to a patient in need thereof a pharmaceutically effective amount of a compound of any one of claims 1, 56 or 57.

2. Level of skill in the art

As the Examiner noted, the skill in the art of chemical synthesis is high. That skill, together with the instant specification, including cited and incorporated references, allow the skilled artisan to make any and all of the claimed compounds. The Examiner went on to note that "the level of skill in the medicinal arts is moderate because it is unclear which if any of the compounds disclosed herein are active against one or more specific disease conditions." Office Action at page 5. Applicant respectfully disagrees. The level of skill in the medical arts is high. This is evidenced by the art in this area, which is authored primarily by those with Ph.D. and M.D. degrees and is intended for an audience of similarly highly skilled individuals, primarily in the fields of biochemical, pharmaceutical, or medical arts. The numerous articles and patents made of record in this application, authored and reviewed by those known in the art, address a highly skilled audience, and further evidence the high level of skill in this art. Therefore, the amount of disclosure required to meet the enablement requirement is minimal.

3. The amount of direction or guidance presented and the presence or absence of working examples.

The specification provides a general description of non-steroidal compounds that are high-affinity, high-specificity agonists, partial agonists (i.e., partial activators and/or tissue-specific activators) and antagonists for androgen receptors (AR). The claimed subject matter is directed to androgen receptor modulator compounds, pharmaceutical compositions containing such compounds as well as methods of using such compounds and pharmaceutical compositions for modulating processes mediated by steroid receptors. The application discloses methods of making such compounds and pharmaceutical compositions, as well as intermediates used in their synthesis. The specification describes seven generic synthesis schemes (for example, see page 33, 35, 37, 38, 39, 41 and 42). One of skill in the art can readily follow these schemes or known variations of such schemes with any of a vast number of commonly available starting materials to arrive at the claimed subject matter. The application names over 150 exemplary AR modulator compounds (for example, see page 29 through 32 and claims 56 and 57.

The specification also provides over 50 working examples. Hence the specification provides a variety of examples of compounds that fall within the scope of the claims evidencing that the claimed compounds function as claimed. The specification also provides two screening assays. As discussed above, various screening assays for assessing the ability of a compound or composition to modulate the transcriptional ability of intracellular receptors are known to those of skill in the art, such as those described in U.S. Pat. Nos. 4,981,784, 5,071,773, 5,298,429, and 5,506,102 and in WO89/05355, WO91/06677, WO92/05447, WO93/11235, WO93/23431, WO94/23068, WO95/18380 and CA 2,034,220. The requirements of 35 U.S.C. §112, first paragraph, do not require a specific example of everything within the scope of the claims. *In re Anderson*, 176 USPQ 331, 333 (CCPA 1973) :

> ...we do not regard section 112, first paragraph, as requiring a specific example of everything within the scope of a broad claim . . . What the Patent Office is here apparently attempting is to limit all claims to the specific examples, not withstanding the disclosure of a broader invention. This it may not do.

In re Grimme, Keil and Schmitz, 124 USPQ 449, 502 (CCPA 1960) :

> It is manifestly impracticable for an applicant who discloses a generic invention to give an example of every species falling within it, or even to name every such species. It is sufficient if the disclosure teaches those skilled in the art what the invention is and how to practice it.

Hence there is no requirement for the applicant to exemplify or even provide an example of everything within the scope of the claims. The Patent Office cannot "limit all claims to the specific examples, notwithstanding the disclosure of a broader invention."

4. Predictability of the art.

The art of chemical synthesis is predictable and is dictated by recognized chemical reactions and constraints. The medical arts are also predictable, in that various assays and models that mimic an *in vivo* system in the laboratory were available and known to the skilled artisan at the time of filing of the application. For example, see U.S. Pat. No. 5,071,773 to Evans *et al.* (1991), which teaches a bioassay for evaluating whether compounds are functional ligands for receptor proteins. Such assays are routine in the medical arts. Thus, it is not necessary that one skilled in the art be able to predict which compound will be most active for a particular medical application. The specification, in view of the skill in the art, describes how to make and administer, and if necessary test, any claimed compound. As discussed above, the level of knowledge and skill in the preparation, isolation, manipulation and compounds was high as of the filing date of the instant application. Therefore, in view of the teachings of the specification, in combination with what was known at the time the original application was filed, applicant respectfully submits that the claimed compounds can be prepared predictably using any methods that are known to those skilled in this art. Further, formulating such compounds into a pharmaceutical composition and administration of such compositions to a subject is well know in the medical arts. Thus, preparation and administration of pharmaceutical compounds is also predictable.

5. The amount of experimentation required.

There is nothing of record to suggest that production or use of any of the claimed compounds or compositions would require development of new procedures or excessive experimentation. Organic synthesis methods have been used for decades. As discussed above, bioassays for evaluating whether compounds are functional ligands for receptor proteins were known in the art since at least 1991. Such assays are routine in this art and do not require excessive experimentation. It is noted that the test for undue experimentation "is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine . . ." *In re Wands* 858 F.3d 731, 737 (Fed Cir. 1988). Thus, methods for making and evaluating androgen receptor modulator compounds were available and known to skilled artisans at the time of filing the application. Those skills, together with the teaching of the specification, including cited and incorporated references, allow the skilled artisan to

make any and all of the claimed compounds. As discussed, it is not necessary that one skilled in the art be able to predict which compound will be most active for a particular medical application. The specification, in view of the skill in the art, enables one to make and administer, and if necessary test, any claimed compound

CONCLUSION

In light of the scope of the claims, the teachings in the specification, the high level of skill of those in this art, the working examples, and the extensive knowledge of those of skill in this art, it would not require undue experimentation for a person skilled in the art to make and use the claimed compounds and compositions. Therefore, the specification is enabling for making and using the full scope of the claimed subject matter. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Policy Considerations

The Examiner is reminded that applicant is entitled to claims that are commensurate in scope not only with what applicant has specifically exemplified, but commensurate in scope with that which one of skill in the art could obtain by virtue of that which the applicant has disclosed. Moreover, it is unfair, unduly limiting and contrary to the public policy and constitutional mandate that underlie the U.S. patent system to require applicant to limit the instant claims to the compounds specifically discussed in the examples. To do so permits one of skill in this art to practice the disclosed invention but avoid liability for infringement merely by selecting a species of the disclosed genus not specifically discussed in the examples.

As a broad body of knowledge is available in the area of chemical, it would be unfair, unduly limiting and contrary to the public policy upon which the patent laws are based to require Applicant to limit these claims to the particular exemplary embodiments. See, e.g., *In re Goffe*, 542 F.2d 801, 166 USPQ 85 (CCPA 1970):

> for the Board to limit appellant to claims involving the specific materials disclosed in the examples so that a competitor seeking to avoid infringing the claims can merely follow the disclosure and make routine substitutions "is contrary to the purpose for which the patent system exists - to promote progress in the useful arts".
>
> The public purpose on which the patent law rests requires the granting of claims commensurate in scope with the invention disclosed. This requires as much the granting of broad claims on broad inventions as it does the granting of more specific claims on more specific inventions. *In re Sus and Schafer*, 49 CCPA 1301, 306 F.2d 494, 134 USPQ 301, at 304.

To require applicant to further limit the claims would permit those of skill in the art to practice what is disclosed in the specification but avoid infringing claims so-limited. To permit

that is simply not fair. The instant application in light of the knowledge of those of skill in the art provides adequate guidance for making and using androgen receptor modulator compounds and compositions. Having done so, it is now routine for others to make minor modifications by any method known in this art. Those of skill in the art should not be permitted to make minor modifications, such as selecting a compound not specifically disclosed in the examples, to avoid infringing such claims.

Rebuttal to Examiner's Arguments

A. Alleged Excessive Breadth of Claims

The Examiner alleges that the "breadth of the compound claims is excessive," asserting that "the term 'may be optionally substituted' without specifying the substituents implied thereby renders the breadth excessive because said term implies that the unnamed substituents is/are open to all possible alternatives" (Office Action at page 4). Applicant respectfully points out that the term "optionally substituted" is defined in the specification at page 11 line 26 to page 12, line 9, which states:

> "Optionally substituted" groups may be substituted or unsubstituted. The substituents of an "optionally substituted" group may include, without limitation, one or more substituents independently selected from the following groups or designated subsets thereof: alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, haloalkenyl, haloalkynyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkoxy, aryloxy, haloalkoxy, amino, alkylamino, dialkylamino, alkylthio, arylthio, heteroarylthio, oxo, carboxyesters, carboxamido, acyloxy, hydrogen, F, Cl, Br, I, CN, NO_2, NH_2, N_3, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CH_3, CF_3, $C(O)CH_3$, CO_2CH_3, CO_2H, $C(O)NH_2$, OR^9, SR^9 and $NR^{10}R^{11}$. An optionally substituted group may be unsubstituted (e.g., $-CH_2CH_3$), fully substituted (e.g., $-CF_2CF_3$), monosubstituted (e.g., $-CH_2CH_2F$) or substituted at a level anywhere in-between fully substituted and monosubstututed (e.g., $-CH_2CF_3$).

Thus, the claims are not unbound as the Examiner asserts. Applicant respectfully requests that the Examiner reconsider the rejection in view of the above.

B. Nature of the Invention

The Examiner alleges that the "nature of the invention includes a method of testing, a method of purification, and a vast number of methods of medicinal treatment" (Office Action at page 4). Applicant respectfully submits that it does not constitute undue experimentation to make, test, and administer any compound of the invention. It is not necessary that one skilled in the art be able to predict precisely which compounds will be the most active for a given disease, because testing compounds in a screening assay, such as the binding assay or the co-transfection assay, both of which are described in the specification, does not constitute undue

experimentation. Indeed, synthesizing and testing compounds is analogous to the process of making and screening antibodies, which the Federal Circuit found **not** to be undue experimentation. *In re Wands* 858 F.3d 731, 8 U.S.P.Q.2d 1400.

C. Specific Disease Conditions

The Examiner alleges that there is no clear showing that compounds that are active as androgen receptor modulators (agonists or antagonists) are actually effective in the treatment of any specific disease condition Office Action page 5). The Examiner requests copies of any art bearing on this topic.

Applicant respectfully submits that at the time of filing the application, use of androgen receptor modulators, such as agonists or antagonists, as therapeutic agents was known to those skilled in the medical arts. For example, Singh *et al.* (*Current Medicinal Chemistry* (2000) **7**: 211-247) teaches that benign prostatic hyberplasia, acne, seborrhea, hirsutism and androgenic alopecia are all well recognized to be sensitive to androgens and to respond to androgen receptor antagonist therapy (page 211, first paragraph). Boyer (*Australian Prescriber* (1996) **19**: 22-24) teaches that steroidal and non-steroidal antiandrogens are used in the hormonal management of prostate cancer amd as part of total androgen blockade. Claman *et al.* (*J Obstet Gynaecol Can* (January 2002) **24**(1): 62-67) teaches androgen suppression and/or androgen recptor blockade for medical treatment of hirsutism and the associated diseases hyperandrogenism and adult-onset congenital adrenal hyperplasia. Copies of these articles are supplied herewith. Thus, there is a clear showing in the art that compounds that are active as androgen receptor modulators are actually effective in the treatment of *many* specific disease conditions.

D. Alleged Limited Direction

The Examiner states that the amount of direction provided is limited to the chemical synthesis of numerous [1,4]oxazino[2,3-*f*]quinolin-8-ones and data identifying which compounds are agonists or antagonists and alleges that no other chemical species has been disclosed as having been synthesized, isolated or subjected to any testing to determine possible medicinal activity. Applicant respectfully disagrees.

The specification teaches seven generic synthesis schemes (for example, see page 33, 35, 37, 38, 39, 41 and 42). The application names over 150 exemplary AR modulator compounds (for example, see page 29 through 32 and claims 56 and 57). The specification also provides over 50 working examples and two screening assays. It is respectfully submitted that the direction provided by the specification is sufficient to allow one of skill in the art to synthesize, test and administer any and all compounds of the claimed subject matter. One

skilled in the art will recognize that the generic schemes may be used to synthesize such compounds, though they may also be synthesized using techniques known to those of skill in the art. Similarly, one of skill in the art may assess certain compounds of the present invention using the binding assay or the co-transfection assay, both of which are disclosed in the specification, though one of skill in the art may assess compounds using other known assays. Finally, administration of compounds is routine to one of skill in the medical arts.

E. Alleged Lack of a Showing of Efficacy of Treatment of a Specific Disease

The Examiner alleges that the specification provides biological testing limited to the compounds noted in the Examples and that the testing was limited "to showings of agonist or antagonist activity in the presence of a receptor, but no showing of efficacy in the treatment of any one of the specific disease conditions listed" (Office Action page 5). The Examiner also states that applicant has shown that the dislcosed compounds have potential utility in the treatment of diease conditions where an androgen-sensitive receptor is implicated but contends that there has been no showing that any particualr disease may be effectively treated using any claimed compound (Office Action pages 5-6).

Applicant is not aware of any requirement under current U.S. patent law specifying particular minimum levels of optimization and certified efficacy in order for an area of art to qualify as sufficiently "predictable" such that lack of enablement under 35 U.S.C. § 112, first paragraph, is not a consideration. The relevant standard is not that of an established, fully optimized, method; rather, even in an unpredictable art, a patent application satisfies the requirements of 35 U.S.C. § 112, first paragraph, as long as it provides sufficient disclosure, either through illustrative examples or terminology, to teach those of skill in the art how to make and use the claimed subject matter without undue experimentation. The teachings of Evans *et al.* (US Pat. Nos. 4,981,784 and 5,071,773 and *Science* **240**:889-95 (1988)) describe a co-transfection assay that mimics an *in vivo* system in the laboratory. Elbrecht *et al.* (U.S Pat. No. 5,872,150) discloses assays for identifying compounds with antiandrogenic activity employing a hamster ductus deferens cell line. Raynaud *et al.*(*J. Steroid Biochem.* **12**:143-157 (1980)) describes a number of steroid hormone receptor competition assays. Tanabe *et al.* (U.S. Pat. No. 5,723,455) descibes a rat prostate androgen receptor competition assay for *in vitro* evaluation of androgen receptor modulator compounds. These references support the teachings of the specification and demonstrate the knowlegde of those of skill in the art at the time the application was filed. These references also provide evidence that those of skill in this art correlate activity in the assays with pharmacological activity. Furthermore,

compounds that have shown activity in these assays (see, *e.g.*, U.S. Patent No. 6,043,279) have shown activity in clinical trials and are now recognized therapeutics.

One of skill in the art would recognize that the assays described in the references and the specification are useful in assessing certain compounds including those presently claimed in the treatment of disease conditions where an androgen-sensitive receptor has been implicated. As discussed above, a number of diseases, including benign prostatic hyberplasia, prostate cancer, acne, seborrhea, hirsutism, hyperandrogenism, adult-onset congenital adrenal hyperplasia and androgenic alopecia, are recognized to be sensitive to androgens and to respond to androgen receptor antagonist therapy. Therefore, compounds that are androgen receptor antagonists, for example, are candidates for clinical use in the treatment of diseases that respond to androgen receptor antagonist therapy.

REJECTION OF CLAIMS 1-7, 9, 11-18, 20, 21, 23-36, 39, 41, 45, 49-51, 56-58, 60-74, 76, 77 AND 86-107 UNDER 35 U.S.C. § 112 SECOND PARAGRAPH

Claims 1-7, 9, 11-18, 20, 21, 23-36, 39, 41, 45, 49-51, 56-58, 60-74, 76, 77 and 86-107 under 35 U.S.C. § 112 second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter. This rejection is respectfully traversed.

RELEVANT LAW

Claims are not read in a vacuum but instead are considered in light of the specification and the general understanding of the skilled artisan. *Rosemount Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 1547, 221 USPQ 1, 7 (Fed. Cir. 1984), *Caterpillar Tractor Co. v. Berco, S.P.A.*, 714 F.2d 1110, 1116, 219 USPQ 185, 188 (Fed. Cir. 1983). A claim is not indefinite when one skilled in the art would understand the language in the claims when read in light of the specification.

35 U.S.C. § 112, second paragraph requires only reasonable precision in delineating the bounds of the claimed invention. Claim language is satisfactory if it reasonably apprises those of skill in the art of the bounds of the claimed invention and is as precise as the subject matter permits. *Shatterproof Glass Corp. v. Libby-Owens Ford Col.*, 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir.), cert. dismissed, 106 S.Ct. 340 (1985).

A. Alleged Incomplete Recitation

The Examiner rejects claims 1-7, 9, 11-18, 20, 21, 23-36, 39, 41, 45, 49-51, 56-58, 60-74, 76, 77, 85, 86, 89, 90, 93, 94, 101 and 102 because the recitation "selected from the group of" allegedly is incomplete because the Examiner urges that Markush groups are

properly formatted using the phrase "selected from the group consisting of" (Office Action at page 6). While use of the term "comprising" instead of "consisting" is not allowed, alternative wording is permitted. MPEP 2173.05(h) (noting that Markush group claims "may be recited in the traditional manner, or alternatively."). The recitation "selected from the group of" reasonably apprises those of skill in the art of the bounds of the claimed subject matter. Hence, the claim language is acceptable. Further, the phrase "selected from the group of" is closed to additional members and, thus, permitted.

B. "Optionally Substituted"

Claims 1-7, 9, 11-18, 20, 21-25, 27-29, 30, 32, 35, 36, 49, 50, 58, 60-62, 64-71, 73 and 74 are rejected because the recitation "may be optionally substituted" is allegedly incomplete because it allegedly fails "to specify the substituents implied thereby." Office Action at pages 6-7. This rejection is respectfully traversed..

As noted above, the term "optionally substituted" is defined in the specification at page 11, line 26 to page 12, line 9, which recites:

> "Optionally substituted" groups may be substituted or unsubstituted. The substituents of an "optionally substituted" group may include, without limitation, one or more substituents independently selected from the following groups or designated subsets thereof: alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, haloalkenyl, haloalkynyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkoxy, aryloxy, haloalkoxy, amino, alkylamino, dialkylamino, alkylthio, arylthio, heteroarylthio, oxo, carboxyesters, carboxamido, acyloxy, hydrogen, F, Cl, Br, I, CN, NO_2, NH_2, N_3, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CH_3, CF_3, $C(O)CH_3$, CO_2CH_3, CO_2H, $C(O)NH_2$, OR^9, SR^9 and $NR^{10}R^{11}$. An optionally substituted group may be unsubstituted (e.g., $-CH_2CH_3$), fully substituted (e.g., $-CF_2CF_3$), monosubstituted (e.g., $-CH_2CH_2F$) or substituted at a level anywhere in-between fully substituted and monosubstututed (e.g., $-CH_2CF_3$).

It is respectfully submitted that one skilled in the art would understand the language in the claims when read in light of the specification. As shown above, the meaning of the recitation "optionally substituted" reasonably apprises those of skill in the art of the bounds of the claimed subject matter. Applicant respectfully requests that the Examiner reconsider the rejection in view of the above.

C. Inadvertant Omission

Claim 61 is rejected because of the inadvertent omission of the term "comprising a compound." Applicant thanks the Examiner for pointing out this error, which is corrected herein. Thus, the rejection is now moot.

D. Claims 87-107

Claims 87-107 are rejected because the Examiner alleges that the term "modulate" is "indefinite for failing to indicate what specific treatment action(s) or effect(s) is(are) intended." It is respectfully submitted that the specification specifically states that "in one aspect, the modulation is activation, while in another aspect, the modulation is inhibition" (see, for example, page 17, lines 4-5). This is in keeping with the use of the term "modulators" throughout the specification, which refer to "compounds that are agonists, partial agonists or antagonists" (see page 1, lines 25-26), where "a compound that binds an IR [intracellular receptor] and mimics the effect of the native ligand is referred to as an "agonist", while a compound that inhibits the effect of the native ligand is called an "antagonist." Thus, when read in light of the specification, one skilled in the art would understand the meaning of the term "modulate" in the claims.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 1-7, 9, 11-14, 16-22, 27, 28, 37, 41, 42, 53, 58-62, 64, 66-68, 73, 75, 80, 82 and 85-107 are rejected as allegedly anticipated by U.S. Pat. Nos. 6,030,967 and 6,340,704 to Marui *et al.* Without acquiescing to the Examiner's allegation and solely to expedite prosecution, claims 1, 32, and 50 are amended herein. Amended claims 1, 32, and 50 are not anticipated by the two Marui *et al.* patents. The remaining rejected claims ultimately depend from those claims. Thus, the rejections under 35 U.S. C. § 102 are moot.

* * *

In view of the above, reconsideration and allowance is respectfully requested.

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 18202-018001 (1082)
Address all correspondence to:
Stephanie Seidman
Fish & Richardson P.C.
12390 El Camino Real
San Diego, California 92130
Telephone: (858) 678-5070
Facsimile: (202) 626-7796
email: seidman@fr.com